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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/763,955
Filing Date: February 28, 2001
Appellant(s): VON BORSTEL, RELD W.

Leonard C. Mitchard
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 2, 2009 appealing from the Office action mailed April 21, 2009.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

Pending appeal in copending application Serial No. 09/930,494, filed August 16, 2001, claims 31-32 and 38-41 of which are the subject of an obviousness-type double patenting rejection with respect to claim 55 of the present application.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Przyrembel J. Inher. Metab. Dis. (1987), Vol. 10, pages 129-146.

DiMauro et al. "Mitochondrial Encephalomyopathies: Where Next?" Revista De Neurologia (1999), Vol. 28, No. 2, pages 164-168.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 48-50, 55, 62-64 and 68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant specification invites the skilled artisan to unduly experiment. Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

The factors include, but are not limited to:

1. The breadth of the claims,
2. The nature of the invention,

3. The state of the prior art,
4. The level of one of ordinary skill,
5. The level of predictability in the art,
6. The amount of direction provided by the inventor,
7. The existence of working examples, and
8. The quantity of experimentation needed to make and/or use the invention based on the content of the disclosure.

Breath of Claims

Claims 48-50, 55, 62-64 and 68 are drawn to a method for treating congenital mitochondrial diseases.

Nature of Invention

This invention relates generally to compounds and methods for treatment and prevention of diseases, developmental delays, and symptoms related to mitochondrial dysfunction. Pyrimidine nucleotide precursors are administered to a mammal, including a human, for the purpose of compensating for mitochondrial dysfunction and for improving mitochondrial functions. It is an object of this invention to provide a practical treatment for mitochondrial diseases that is beneficial in the case of mitochondrial electron transport chain deficits regardless of the specific molecular defects.

State of the Prior Art

At the time of the invention, the treatment of mitochondrial disorders was ineffective. There were no correlations between treatment regimens and therapeutic

responses to disorders. Treatment was unpredictable and heterogenous. The examiner directs applicant to PRZYREMBEL *J. Inher. Metab. Dis.* (1987), Vol. 10, pages 129-146 (PRZYREMBEL). PRZYREMBEL teaches, "Mitochondrial disorders, namely defects of fatty acid oxidation, defects of pyruvate metabolism and defects of the respiratory chain are heterogenous in clinical picture and in response to therapeutic attempts. Defects of fatty acid metabolism are amenable to therapy by dietary means, carnitine substitution and in some cases with vitamins. Defects in pyruvate metabolism do not respond to therapy except in some special cases. Therapeutic attempts include dietary measures, vitamins as coenzyme precursors. Defects in the respiratory chain appear to respond to treatment only in exceptional cases. Evaluation of treatment effects appears to be singularly difficult." See Abstract.

Level of Ordinary Skill in the Art

The level of skill in the art is seen to be a M.D. specializing in mitochondrial disorders or a PhD in the field of biomedical research.

Level of Predictability in the Art /Amount of Direction Provided by the Inventor

Please note that a single embodiment may provide broad enablement in cases involving predictable factors, but more is required in cases involving unpredictable factors, such as chemical or physiological activity, see *Ex. parte Hitzeman*, 9 USPQ2d 1821. The working examples in the specification are limited to the use of triacetyluridine for treating mitochondrial disorders. One of skill in the art at the time of the instant invention would have predicted that no single compound or family of compounds would

have been effective for the treatment of the broad spectrums of mitochondrial disorders instantly claimed. Additionally, due to the extreme difficulty in treating mitochondrial disorders, one of ordinary skill would have set a very high bar in accessing whether treatment was successful. PRZYREMBEL teaches, "Patients with defects in mitochondrial function are difficult to treat with our available means. When treatment is considered it has to start early and should be aggressive and run parallel to diagnostic procedures on an experimental basis…Defects in the respiratory chain appear to respond to treatment only in exceptional cases. Evaluation of treatment effects appears to be singularly difficult."

In addition to the teachings of PRZYREMBEL, as set forth supra, the specification teaches, "while useful in isolated cases, no such metabolic cofactors or vitamins have been shown to have general utility in clinical practice in treating mitochondrial diseases. Similarly, dichloracetic acid (DCA) has been used to treat mitochondrial cytopathies such as MELAS; DCA inhibits lactate formation and is primarily useful in cases of mitochondrial diseases where excessive lactate accumulation itself is contributing to symptoms. However, DCA does not address symptoms related to mitochondrial insufficiency per se and can be toxic to some patients, depending on the underlying molecular defects…Mitochondrial diseases comprise disorders caused by a huge variety of molecular lesions or defects, with the phenotypic expression of disease further complicated by stochastic distributions of defective mitochondria in different tissues." See pages 2-3 of the specification.

Working Examples / Quantity of Experimentation Needed to make and/or use the Invention Based on the Content of the Disclosure

The working examples on pages 40-49 have been noted. The examples are limited to the use of triacetyluridine. Example 3 is directed to the treatment of renal tubular acidosis. The subject (2 year-old girl) had Leigh's Syndrome; however, the example does not suggest the efficacious treatment of Leigh's Disease. Example 8 is directed to the therapeutic effect of triacetyluridine in the 3-nitropropionic acid model of Huntington's disease. These examples are not sufficient to support applicant's claim of the treatment of the instantly claimed disorders. PRZYREMBEL teaches, "Therefore recommendations about what to do with an individual patient with a specific defect will be relatively vague. Evaluation of the effect of any chosen treatment regimen is also problematic. Many mitochondrial encephalomyopathies tend to show an episodic course. Acute attacks, leading to neurological deficits, and spontaneous recovery follow each other. Recovery, however, is in most cases only partial and a progressive downhill course is the result." See pages 129-130.

2. Claim 55 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 31-32 and 38-41 of copending Application No. 09/930,494.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

(10) Response to Argument

1. Applicant argues that Przyrembel was published eight years before the priority date of the present application and at a very early stage in the understanding of mitochondrial diseases and their treatment. In support of applicant's position, DiMauro et al. is cited. Applicant contends that DiMauro notes the "enormous progress" made since Luft's initial work; however, applicant concedes that the DiMauro reference was published about a year after the priority date of the subject application.

The examiner respectfully disagrees with applicant's characterization of DiMauro. Although DiMauro teaches that progress has been made, in regards to therapy, DiMauro teaches, "To the frustration of…doctors, therapy of respiratory chain disorders remains woefully inadequate and usually limited to the administration of various vitamins and cofactors. Gene therapy is still a distant possibility for nuclear defects and is daunting for mtDNA gene defects...there are some promising experimental approaches, but therapy in general remains a major challenge for future researches." See page 180. The teachings of DiMauro and Przyrembel are consistent in regards to the lack of an effective treatment regimen for mitochondrial diseases at the time of the instant invention. The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date. Publications dated after the filing date providing information publicly first disclosed after the filing date generally cannot be used to show what was known at the time of filing.

2. Applicant has failed to set forth arguments as to why the provisional rejection is improper but has indicated a willingness to consider filing a Terminal Disclaimer when otherwise allowable subject matter is indicated.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Patrick T. Lewis/

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